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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/762,439	ASHTON ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,16-18,20 and 21* is/are pending in the application.

4a) Of the above claim(s) *4-9 and 11-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 10, 14, 16-18 and 20-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments, filed on 06/06/08 and the Request for Continued Examination filed on 12/19/08 are acknowledged.

2. Claims 4-9 and 11-13 were withdrawn.

3. Claims 1-2, 10, 14 and 18 were amended. Claims 15 and 19 were cancelled.

4. Claims 1-3, 10, 14, 16-18, and 20-21 are included in the prosecution.

Continued Examination under 37 CFR 1.114

5. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/19/08 has been entered.

Response to Arguments

Rejection of claims 1-3, 10, 14, and 16-17 under 35 USC § 103(a)

6. Applicants' arguments see Page 7, filed 06/06/08, with respect to the rejection of claims 1-3, 10, 14, and 16-17 under 35 USC § 103(a) as being unpatentable over Smith et al. (US 5,378,475) in view of Wong et al. (US 6,331,313) have been fully considered. In light of the amendments to claims 1-2 and 14, that include the limitation of the one or more additional coating layers that comprise an adrenergic agent that is the same or different as the adrenergic agent of the inner drug core, the rejection of 01/04/08 is

withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Smith et al. (US 5,378,475) in view of Wong et al. (US 6,331,313) and further in view of Heller et al. (US 3,811,444).

Rejection of claims 18 and 20-21 under 35 USC § 103(a)

7. Applicants' arguments see Page 9, filed 06/06/08, with respect to the rejection of claims 18 and 20-21 under 35 USC § 103(a) as being unpatentable over Chen et al. (US 5,902,598) in view of Wong et al. (US 6,331,313) have been fully considered. In light of the amendments to claim 18, that includes the limitation of the one or more additional coating layers that comprise an adrenergic agent that is the same or different as the adrenergic agent of the inner drug core, the rejection of 01/04/08 is withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Chen et al. (US 5,902,598) in view of Wong et al. (US 6,331,313) and further in view of Heller et al. (US 3,811,444)

8. In addition, a provisional obviousness type double patenting rejection is being made against the claims of co-pending Application No. 10/762,421.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1-3, 10, 14, 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (US 5,378,475) in view of Wong et al. (US 6,331,313) and further in view of Heller et al. (US 3,811,444).

The claimed invention is a sustained release drug device adapted for implantation in or adjacent to the eye of a patient, the drug delivery device comprising: (i) an inner drug core comprising an adrenergic agent and a matrix material wherein said adrenergic agent is admixed in the matrix material to inhibit or prevent decomposition of the adrenergic agent; (ii) a first coating on the surface of the drug core, that is substantially impermeable to the passage of the adrenergic agent, having one or more openings therein which permit diffusion of the adrenergic agent, and which is substantially insoluble and inert in body fluids and compatible with body tissues; and (iii) one or more additional coatings that are permeable to the passage of the adrenergic agent, are substantially insoluble and inert in body fluids and compatible with body tissues and comprise an adrenergic agent that is the same or different as the adrenergic agent of the inner drug core; wherein the first and additional coatings are disposed about the inner drug core so as to produce, when implanted, a substantially constant rate of release of the adrenergic agent from the device.

Smith teaches a sustained release drug delivery device including an inner core or reservoir with the active ingredient and coating layers (Abstract). The first coating layer is “essentially impermeable to the passage of the effective agent, and a second coating permeable to the passage of the effective agent” (Col. 1, lines 6-12). The invention includes “an ocular device suitable for direct implantation into the vitreous of the eye”

which provides "sustained controlled release of various compositions to treat the eye without risk of detrimental side effects" (Col. 3, lines 38-43). Further, Smith teaches that "the devices are particularly suitable for treating ocular conditions such as glaucoma" (Col. 5, lines 28-29). Antiglaucoma adrenergic drugs such as timolol and betaxolol are disclosed as components of the inner core of the device (Col. 5, lines 51-52).

Smith does not expressly teach a bioerodible polymer matrix in the core mixed with the adrenergic agent.

Wong teaches a controlled release biocompatible ocular drug delivery device that can be implanted in the eye (Abstract). The device comprises "a substantially impermeable polymeric outer layer covering a core which comprises the drug to be delivered …" (Col. 1, lines 56-59). The device "is implanted in the eye to treat or prevent a variety of conditions of the eye such as … ocular pressure…" (Col. 8, lines 12-15). Wong, teaches that the drug "may also be present as a solution or be dispersed in a polymer matrix. The polymers used in the matrix with the drug are bio-compatible with body tissues and body fluids and can be biodegradable or substantially insoluble in the body fluids" (Col. 10, lines 35-39). Biodegradable polymers that can be used with the drug in the core are disclosed (Col. 9, line 60 to Col. 10, line 9).

Smith and Wong do not expressly teach an outer or second layer comprising an adrenergic agent that is the same or different as the adrenergic agent of the inner drug core.

Heller teaches an ocular insert for the continuous controlled administration of a therapeutically effective dosage of drug to the eye over a prolonged period of time (Abstract). Figure 4 illustrates a bioerodible ocular insert comprised of a series of three concentric layers where the outer layer comprises particles of drug (Col. 13, lines 5-12). Heller teaches that "many variations of the device of FIG. 4 will be apparent to those skilled in the art of drug delivery. For example … a variety of drugs or dosages may be employed in the several layers ..." (Col. 13, lines 27-33). Heller teaches epinephrine (an adrenergic agent) that is a suitable drug for use in the ocular insert (Col. 14, lines 30-54).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the sustained release drug delivery device for an ocular implant, as suggested by Smith, combine it with the implantable ocular drug delivery device including an adrenergic agent and a bioerodible polymer matrix core, as suggested by Wong, further combine it with the outer layer of an ocular insert that comprises a drug, as suggested by Heller, and produce the instant invention.

One of ordinary skill in the art would do this because Smith teaches using the device for treating glaucoma and Wong teaches using the device for treating high ocular pressure and includes specific adrenergic agents. One of ordinary skill in the art would use adrenergic agents in the device to treat high ocular pressure that is associated with glaucoma. As mentioned earlier, the device allows sustained controlled release of the active "without risk of detrimental side effects" (Col. 3, lines 40-43). One of ordinary skill in the art would find it obvious to incorporate a drug in the outer layer of the sustained

release drug device in order to provide immediate release of the drug. Variable drug release from the outer layer of an ocular insert is evidenced by the teaching of Heller (Col. 13, lines 5-33).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claims 1-2 and 14 the limitations of a sustained release drug delivery device for implantation in the eye, an inner core comprising an adrenergic agent, a first coating that is substantially impermeable to the passage of the adrenergic agent, one or more additional coatings that are permeable to the passage of the adrenergic agent would have been obvious over the sustained release drug delivery device for an ocular implant teaching of Smith in view of the adrenergic agents and the drug in the bioerodible polymer matrix, as taught by Wong. Smith teaches a first coating layer that is “essentially impermeable to the passage of the agent” and a second coating layer that is “permeable to the passage of the agent” (Col. 3, lines 15-29). The first coating layer being impermeable to the passage of the agent controls “the release of the agent out of the drug delivery device” (Col. 7, lines 10-15). The limitation of the adrenergic agent admixed in the matrix material would have been obvious over the teaching by Wong that the drug “may also be present as a solution or be dispersed in a polymer matrix. The polymers used in the matrix with the drug are bio-compatible with

body tissues and body fluids and can be biodegradable or substantially insoluble in the body fluids" (Col. 10, lines 35-39). Biodegradable polymers that can be used with the drug in the core are disclosed (Col. 9, line 60 to Col. 10, line 9). When the adrenergic agent is mixed with a substantially insoluble polymer and the mixture is present in the core, one of ordinary skill in art would expect to inhibit or prevent the decomposition of the adrenergic agent with a reasonable expectation of success. The limitation of an outer or second layer comprising an adrenergic agent that is the same or different as the adrenergic agent of the inner drug core would have been obvious over the outer layer of an ocular insert that comprises a drug, and over the epinephrine suggested by Heller (Col. 13, lines 5-33).

The limitations of the impermeable coating having sufficient dimensional stability of instant claims 2 and 3 would have been obvious over the teaching in Smith that "devices formed of polymeric materials that are insoluble in tear fluid retain their shape and integrity during the course of the needed therapy …" (Col. 2, lines 18-21). "Materials that may be suitable for fabricating the fist or second coating layer of the device include naturally occurring or synthetic materials that are biologically compatible with body fluids and eye tissues, and essentially insoluble in body fluids with which the material will come in contact" (Col. 6, lines 30-35). Therefore, a person having ordinary skill in the art would find that an ocular implant device comprised of coating materials that are insoluble in eye fluids would retain its shape and integrity during the course of therapy.

The limitation of the adrenergic agent of instant claim 10 would have been obvious over the timolol and betaxolol disclosed as components of the inner core of the device by Smith (Col. 5, lines 51-52) and over the epinephrine taught by Heller (Col. 14, lines 30-54).

Regarding instant claim 16, the limitation of the bioerodible polymer matrix would have been obvious over the teaching by Wong that the drug "may also be present as a solution or be dispersed in a polymer matrix. Wong also teaches examples of biodegradable polymers that can be used in the device where "the outer layer degrades after the drug has been released for the desired duration" (Col. 9, lines 43-45 and lines 60-67, Col. 10, lines 1-9).

Regarding instant claim 17, the limitation of co-extruding the inner drug core and the coating layer would have been obvious over the method of extrusion used to prepare the devices and the outer layers, as taught by Wong (Col. 14, line 65 to Col. 15, line 2). It is noted that the instant claim 17 is set forth in the form of product-by-process claims, which are considered product claims by the Office. Applicants are reminded that process limitations cannot impart patentability to a product that is not patentably distinguished over the prior art. In *re Thorpe et al.* (CAFC 1985), supra; In *re Dike* (CCPA 1968) 394 F2d 584, 157 USPQ 581; Tri-Wall Containers, Inc. v. United States et al. (Ct Cls 1969) 408 F2d 748, 161 USPQ 116; In re Brown et al. (CCPA 1972) 450 F2d 531, 173 USPQ 685; Ex parte Edwards et al. (BPAI 1986) 231 USPQ 981.

11. Claims 18 and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (US 5,902,598) in view of Wong et al. (US 6,331,313) and further in view of Heller et al. (US 3,811,444).

Chen teaches sustained release drug delivery devices "suitable for treating ailments affecting the eye" (Col. 2, lines 5-6). Chen discloses an "ocular device suitable for direct implantation into the vitreous of the eye" which provides "sustained controlled release of various compositions to treat the eye without risk of detrimental side effects" (Col. 4, lines 6-11). The "device includes an inner core or reservoir which contains an agent effective in obtaining a desired effect. The device further includes a first coating layer, a second coating layer and a third coating layer. The first coating layer … is permeable to the passage of the effective agent …" (Col. 4, lines 53-58). The device is "particularly suitable for treating ocular conditions such as glaucoma …" (Col. 5, lines 65-66). Chen teaches antiglaucoma drugs such as the beta-blockers timolol and betaxolol (Col. 6, lines 5-19).

Chen does not expressly teach an outer or second layer comprising an adrenergic agent that is the same or different as the adrenergic agent of the inner drug core.

The teaching of Wong (with respect to biodegradable polymers that can be used with the drug in the core) is stated above. Wong also teaches the drugs timolol, betaxolol and epinephrine that may be used in the ocular device (Col. 10, lines 55-60 and Col. 11, line 18).

Chen and Wong do not expressly teach an outer or second layer comprising an adrenergic agent that is the same or different as the adrenergic agent of the inner drug core.

The teaching of Heller (with respect to the outer layer of an ocular insert that comprises a drug) is stated above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the sustained release drug delivery device for an ocular implant including drugs such as adrenergic agents timolol and betaxolol, as suggested by Chen, combine it with the implantable ocular drug delivery device including adrenergic agents (beta blockers) and a bioerodible polymer matrix core, as suggested by Wong, further combine it with the outer layer of an ocular insert that comprises a drug, as suggested by Heller, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Chen teaches using the device for treating glaucoma and Wong teaches using the device for treating high ocular pressure and includes beta blockers as the drugs that may be used. One of ordinary skill in the art would use the adrenergic agents in the device to treat high ocular pressure that is associated with glaucoma. Chen teaches a device that allows sustained controlled release of the active “without risk of detrimental side effects” (Col. 4, lines 6-11). One of ordinary skill in the art would find it obvious to incorporate a drug in the outer layer of the sustained release drug device in order to provide immediate release of the drug. Variable drug release from the outer layer of an ocular insert is evidenced by the teaching of Heller (Col. 13, lines 5-33).

Regarding instant claim 18 the limitations of a sustained release drug delivery device for implantation in the eye, an inner core comprising an adrenergic agent, a first coating that is substantially impermeable to the passage of the adrenergic agent, one or more additional coatings that are permeable to the passage of the adrenergic agent would have been obvious over the sustained release drug delivery device for an ocular implant teaching of Chen in view of the adrenergic agents and the drug in the bioerodible polymer matrix, as taught by Wong. The limitation of the adrenergic agent admixed in the matrix material would have been obvious over the teaching by Wong that the drug "may also be present as a solution or be dispersed in a polymer matrix. The polymers used in the matrix with the drug are bio-compatible with body tissues and body fluids and can be biodegradable or substantially insoluble in the body fluids" (Col. 10, lines 35-39). Biodegradable polymers that can be used with the drug in the core are disclosed (Col. 9, line 60 to Col. 10, line 9). When the adrenergic agent is mixed with a substantially insoluble polymer and the mixture is present in the core, one of ordinary skill in art would expect to inhibit or prevent the decomposition of the adrenergic agent with a reasonable expectation of success. The limitation of an outer or second layer comprising an adrenergic agent that is the same or different as the adrenergic agent of the inner drug core would have been obvious over the outer layer of an ocular insert that comprises a drug, as suggested by Heller (Col. 13, lines 5-33).

Regarding instant claim 20, the limitation of the bioerodible polymer matrix would have been obvious over the teaching by Wong that the drug "may also be present as a solution or be dispersed in a polymer matrix. Wong also teaches examples of

biodegradable polymers that can be used in the device where "the outer layer degrades after the drug has been released for the desired duration" (Col. 9, lines 43-45 and lines 60-67, Col. 10, lines 1-9).

Regarding instant claim 21, the limitation of co-extruding the inner drug core and the coating layer would have been obvious over the method of extrusion used to prepare the devices and the outer layers, as taught by Wong (Col. 14, line 65 to Col. 15, line 2). It is noted that the instant claim 21 is set forth in the form of product-by-process claims, which are considered product claims by the Office. Applicants are reminded that process limitations cannot impart patentability to a product that is not patentably distinguished over the prior art. In *re Thorpe et al.* (CAFC 1985), supra; In *re Dike* (CCPA 1968) 394 F2d 584, 157 USPQ 581; Tri-Wall Containers, Inc. v. United States et al. (Ct Cls 1969) 408 F2d 748, 161 USPQ 116; In re Brown et al. (CCPA 1972) 450 F2d 531, 173 USPQ 685; Ex parte Edwards et al. (BPAI 1986) 231 USPQ 981.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d

1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-3, 14, 16-18 and 20-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 14, 16-18 and 20-21 of copending Application No. 10/762,421 (the '421 Application).

Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to a sustained release drug device for implantation in or adjacent to the eye of a patient. The difference is that instant claims are drawn to the drug core comprising an adrenergic agent and claims of the '421 Application are drawn to the drug core comprising a carbonic anhydrase inhibitor. One of ordinary skill in the art would have found it obvious to use different drugs in the

sustained release drug device based on the desired therapeutic effect in the eye. The instant Specification discloses the use of carbonic anhydrase inhibitors from the drug core (as illustrated in Figure 1 and on Page 28, paragraphs 1-3). The instant application discloses the use of carbonic anhydrase inhibitors for the treatment of glaucoma (Pages 1-2).

Since the instant application claims a sustained release drug device for implantation in or adjacent to the eye of a patient, it is obvious over the claims of the '421 Application, and thus they are not patentably distinct over each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/ /MP WOODWARD/
Examiner, Art Unit 1615 Supervisory Patent Examiner, Art Unit 1615